REMARKS

The Specification has been amended to include sequence identification numbers which were omitted at the time of filing.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**".

The undersigned hereby states that the compact disc copy of the Sequence Listing and the computer readable form copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.825(a) and (b), respectively, are the same and contain no new matter. Accordingly, entry of the Sequence Listing into the above-captioned case is respectfully requested.

In the unlikely event that the patent office determines that extensions and/or other relief is required, applicant petition for any required relief including extensions of time and authorize the assistant commissioner to charge the cost of such petitions and/or fees due to our deposit account no. 03-1952 under order no. 399632003300. The assistant commissioner is not authorized to charge the cost of the issue fee to the deposit account.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at page 27, line 10, has been amended as follows:

Figures 11A-B illustrate an exemplary input text file containing user input parameters used for executing a Junctional Analyzer program, in accordance with one embodiment of the invention (SEQ ID NOS: 70-80; SEQ ID NOS: 7-22; SEQ ID NOS: 27-34; SEQ ID NOS: 59-68 and SEQ ID NOS: 341-368).

Paragraph beginning at page 27, line 16, has been amended as follows:

Figures 13A-D illustrate an exemplary output text file containing output results of a Junctional Analyzer program, in accordance with one embodiment of the invention (SEQ ID NOS: 7-22; SEQ ID NOS: 27-34; SEQ ID NOS: 59-68; SEQ ID NOS: 341-368 and SEQ ID NOS: 70-80).

Paragraph beginning at page 27, line 27, has been amended as follows:

Figures 18A-N show the amino acid sequences and nucleic acid sequences of certain multi-epitope constructs (SEQ ID NOS: 81-142).

Paragraph beginning at page 27, line 29, has been amended as follows:

Figures 19A-E show the amino acid sequences for epitopes present in certain multiepitopic constructs (SEQ ID NOS: 143-340).

Paragraph beginning at page 34, line 21, has been amended as follows:

		Flanking	Epitope	Flanking		Responses
Epitope	Minigene	N terminus	Sequence (SEQ ID NOS:1-4)	C-terminus	Frequency	Magnitude 1)
Core 18	pMmin 5	TLKAAA	FLPSDFFPSV	FLLSLG	6/6	5.5
	pMin1	TLKAAA	FLPSDFFPSV	KLTPLC	6/6	1074.5
Core 132	HCV1	ILGGWV	DLMGYIPLV	YLVAYQ	2/12	107.7
	HCV2	VPGSRG	DLMGYIPLV	AKFVA	17/18	929.2

Paragraph beginning at page 42, line 25, has been amended as follows:

The motifs 206 in the text file 200 provide a "mask" or structural model for identifying junctional epitopes. For example the first motif 206a shown in Figure 11, XXXX(FY)XX(LIMV) (SEQ ID NOS: 7-14), defines an epitope that is eight amino acids in length. The value "X" indicates that any amino acid may be at that position of the epitope. The value "(FY)" indicates that either an F amino acid or a Y amino acid may be in the fifth position of the epitope. Similarly, "(LIMV)" indicates that any one of the listed amino acids, L, I, M or V, may be in the eighth position of the epitope. Therefore if a sequence of eight amino acids spanning a junction of two peptides satisfies the above motif criteria, it is identified as a junctional epitope.

Paragraph beginning at page 43, line 32, has been amended as follows:

Figures 13A-D (hereinafter Figure 13) illustrate an exemplary output text file 400 that lists, for each peptide pair, the spacer combination having the maximum function value. In the example shown in Figure 13, eleven peptides, labeled A-K 202 (Fig. 11), were processed, the Motifs 206 were used to detect junctional epitopes, the enhancement weight values for each potential flanking residue 204 were used, and MaxInsertions 208 was set to four. Other

parameters for controlling the operation and format of the Junctional Analyzer program were set as illustrated by the parameter settings 402. For purposes of convenience, in a preferred embodiment, these input parameters are repeated in the output text file 400. The output text file 400 includes an output table 404 which contain the results of steps 305 (Fig. 12). The first column (Col. 1) of the output table 404 indicates the first peptide of a pair. The second column (Col. 2) of the output table lists the first amino acid insertions which function both as a spacer and the C+1 flanking amino acid. The third column lists a second spacer amino acid. The fourth column lists a third spacer amino acid. The fifth column lists a fourth spacer amino acid which is also the N-1 flanking amino acid for the second peptide of the pair which is listed in column six. The seventh column lists the enhancement weight value of the C+1 flanking amino acid listed in column two. The eighth column lists the enhancement weight value of the N-1 flanking amino acid listed in column six 412. The ninth column lists the sum of the C+1 and N-1 enhancement weight values. The tenth column lists the number of junctional epitopes found in the peptide pair and the eleventh column lists the maximum function value for the peptide pair based on the equations listed above. For example, the first row of the output table 404 shows that for the peptide pair A-B, corresponding to the peptides VLAEAMSQV - ILKEPVHGV (SEQ ID NOS: 5-6), the spacer combination of three amino acids, CAL, eliminates all junctional epitopes and provides a maximum function value of 8.80. It is understood, however, that other output options may be implemented in accordance with the invention. For example, the output table 404 may show the top 32 results for each pair of peptides, or show every result for all possible insertions in the order evaluated, or trace the motif search process to generate large output files, depending on the level of detail and/or analysis desired by the user.

Paragraph beginning at page 78, line 6, has been amended as follows:

Optimized constructs were designed with the aid of the computer assisted methods described above which simultaneously minimize the formation of junctional epitopes and optimize C+1 processing efficiency. The following motifs were utilized for junctional minimization: murine K^b [XXXX(FY)X_{2-3}(LIMV)](SEQ ID NOS: 7-22); D^b [XXXXNX_{2-3}LIMV)](SEQ ID NOS: 23-30); human A2 [X(LM)X_{6-7}V](SEQ ID NOS: 31-34); human A3/A11 [X(LIMV)X_{6-7}(KRY)](SEQ ID NOS:35-58); and human B7 [XPX_{6-7}(LIMVF)](SEQ ID

NOS:59-68). The C+1 propensity values were calculated from the data presented in Figure 6 and are as follows: K = 2.2; N = 2; G = 1.8; T = 1.5; A,F,S = 1.33; W,Q = 1.2; R = 1.7; M,Y = 1; I = 0.86; L = 0.76; V,D,H,E,P = 0. Insertion of up to four amino acids was permitted. Examples of constructs designed by this procedure and other procedures set forth herein are depicted in Figure 19. A number of these constructs were characterized *in vitro* and *in vivo* immunogenicity studies, which are set forth hereafter. Figure 20 lists amino acid epitope sequences encoded by certain nucleic acid sequences set forth in multiepitopic constructs.

Paragraph beginning at page 79, line 29, has been amended as follows:

The ability of multiepitope HTL DNA-based constructs to induce an HTL response *in vivo* was evaluated by intramuscular immunization of $H2^{bxd}$ mice with an HIV-1043-PADRE construct. The HIV-1043-PADRE construct is set forth in Figure 19, and the difference between HIV-1043-PADRE and HIV-1043 is that the former includes a C-terminal GPGPG spacer followed by the PADRE sequence AKFVAAWTLKAAA (SEQ ID NO: 69). Eleven days after immunization, no booster immunizations were administered, CD4 T cells were purified from the spleen, and peptide specific HTL responses were measured in a primary γ-IFN ELISPOT assay. Examples of HTL activity induced by constructs encoding HIV epitopes are shown in Figure 17. Overall, the HTL responses induced by DNA immunization with the multiepitope HIV HTL construct were generally of equal or greater magnitude than the responses induced by peptide immunization.